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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/823,257 03/30/2001 John E. Landers P0715/7003(HCL) 7247

7590 06/16/2003

Helen C. Lockhart, Esq.  
c/o Wolf, Greenfield & Sacks, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, MA 02210-2211

EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/823,257	LANDERS, JOHN E.
	Examiner	Art Unit
	Jeanine A Goldberg	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 27 March 2003.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1-64 is/are pending in the application.

4a) Of the above claim(s) 29-64 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-28 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 0303.

4) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_

**DETAILED ACTION**

1. This action is in response to the papers filed March 27, 2003. Currently, claims 1-64 are pending. Claims 29-64 have been withdrawn as drawn to non-elected subject matter.
2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.
3. Any objections and rejections not reiterated below are hereby withdrawn in view of Applicant's response.

***Maintained Rejections***

***Election/Restrictions***

4. Applicant's election with traverse of Group I, Claims 1-28 in Paper filed March 21, 2003 is acknowledged. The traversal is on the ground(s) that a search and examination of the other groups would not place an undue burden on the Examiner. This is not found persuasive because each of the groups requires different method steps, different reagents.

Claims 29-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed March 21, 2003.

This application contains claims 29-64 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The requirement is still deemed proper and is therefore made FINAL.

***Priority***

5. This application claims priority to provisional application 60-194,425, filed April 4, 2000.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in–  
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or  
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

6. Claims 1-4, 6-7, 11, 14, 16, 18-19, 22-23, 25-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Gentalen et al. (US Pat. 6,306,643, October 2001).

Gentalen teaches a method of using an array of probes in genetic analysis.

Gentalen teaches methods which use multiple cells in an array containing different

pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55)(limitations of Claim 1, 2, 3, 4, 11, 14, 22, 23). The supports typically have discrete spatially addressable regions or cells (col. 11, liens 15-16). (limitations of Claim 6, 7). The target nucleic acid can be genomic, mitochondrial DNA, RNA or cDNA (col. 10, lines 19-20, col. 6, lines 33-34)(limitations of Claim 25-28). The genomic DNA samples are usually subject to amplification before application to an array (col. 10, lines 22-23)(limitations of Claims 16-17). Methods which amplify genomic DNA samples prior to application to the array have reduced the complexity of the genome.

### **Response to Arguments**

The response traverses the rejection. The response asserts Gentalen does not disclose each element of the pending claims. The response asserts that because Gentalen uses pooled probes, identification of a single SNP is not allowed (page 2, Response filed March 21, 2003). The response asserts that the claims require a method which involves capturing a nucleic acid on a surface to identify a first allele of the first SNP and separately analyzing a second SNP. This argument has been reviewed but is not convincing because the claims are broadly drawn to a method using open claim language, namely comprising. Furthermore, as exemplified in dependant

Claim 14, the alleles of the second SNP may be analyzed simultaneously with one another. Therefore, the limitation that the SNPs are separately analyzed, is encompassed by the method taught by Gentalen. Furthermore, as seen in Figure 2, a method of detecting two different probe sequence at the same address on the oligonucleotide array. While Gentalen illustrates that individual targets hybridize less strongly than linked targets, which hybridize cooperatively, the claim does not exclude this embodiment. Additionally, Gentalen teaches the hybridization of two separate molecules. Figure 3, c, illustrates a design and layout of a paired probe array which contain different combinations of the two probes. Figure 5 illustrates the cooperative hybridization and assignment of linkage between SNPs separated by various differences. It is clear from the Figure that each allele of both of the positions are analyzed separately, but simultaneously. Since each position is determined using the array, each position is analyzed separately. Thus for the reasons above and those already of record, the rejection is maintained.

**New Grounds of Rejection**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-4, 6-7, 11, 14, 16, 18-22, 25, 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sapolsky et al (US Pat. 5,858,659, January 1999) in view of Murphy et al. (WO 99/09164, February 25, 1999).

Sapolsky et al. (herein referred to as Sapolsky) teaches a rapid efficient method for analyzing polymorphic markers using arrays (abstract). The arrays of Sapolsky are arranged in blocks which are capable of discriminating the three genotypes for a gene marker. Sapolsky teaches that providing a genetic linkage map allows one to identify a set of genetic markers that follow a specific trait (col. 1, lines 30-35). Sapolsky teaches the use of polymorphisms as genetic linkage markers is of critical importance in locating, identifying and characterizing the genes which are responsible for specific traits (col. 1, lines 65-68). The arrays of oligonucleotides allows for screening large numbers of polymorphic markers in a genome (col. 2, lines 10-15). As seen in Figure 2, a single oligonucleotide array contains 78 separate detection blocks. The triplet layout of detection blocks for the polymorphism is illustrated. The tiled arrays include a number of detection blocks which are specific and complementary to each variant (col. 5, lines 20-26). The probes are synthesized in pairs differing at the biallelic base (col. 5, lines 25-28). Once an array is tiled for a set of polymorphisms, the target nucleic acid is hybridized with the array and scanned (col. 6, lines 5-15). Sapolsky demonstrates detection of DNA and RNA (col. 11-12). Sapolsky teaches the advantages of the method allow for rapid, automatable analysis of genetic linkage to even complex polygenic traits.

Sapolsky does not specifically teach that the method may be used on haplotypes.

However, Murphy et al. (herein referred to as Murphy) teaches a method of using DNA chips to immobilize oligonucleotides on a solid support to rapidly analyzed gene and their expression. Murphy describes a chip having "n" elements for performing allele specific sequence based techniques which has "n" different nucleotide sequences. The oligonucleotides of the chip are capable of specifically hybridizing to a haplotype of the BRCA2 DNA where at least one oligonucleotide is capable of specifically hybridizing to at each of the nucleotide positions recited. Table III, pages 38-39, contain the various haplotypes of BRCA2.

Therefore, it would have been *prima facie* obvious to one of ordinary skill at the time the invention was made to have used the SNP detection method of Sapolsky for detecting haplotypes comprising multiple SNP regions as taught by Murphy. While Sapolsky specifically suggest that analysis of multiple sets of markers in genetic linkage, Sapolsky does not explicitly teach analysis of specific SNPs which form a haplotype. However, Murphy specifically teaches five different haplotypes within the BRCA2 gene which contain various combinations of nucleotides. Murphy teaches a chip may be used to analyze the polymorphisms. Therefore, using the rapid, automatable analysis method of Sapolsky to detect specific combinations of SNPs which form a haplotype would have been obvious to the skilled artisan. Haplotypes have been found to contain more information than individual SNPs. Therefore, the

ordinary artisan would have been motivated to have detected haplotypes using allele specific oligonucleotides on arrays.

8. Claims 5, 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over or Sapolksy et al (US Pat. 5,858,659, January 1999) in view of Murphy et al. (WO 99/09164, February 25, 1999) as applied to Claims 1-4, 6-7, 11, 14, 16, 18, 19-22, 25, 27 above or Gentalen et al. (US Pat. 6,306,643, October 2001) in view of Newton (U.S. Patent 5,525,494, June 11, 1996).

Gentalen teaches a method of using an array of probes in genetic analysis. Gentalen teaches methods which use multiple cells in an array containing different pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55)(limitations of Claim 1, 2, 3, 4, 11, 14, 22, 23). The supports typically have discrete spatially addressable regions or cells (col. 11, lines 15-16). (limitations of Claim 6, 7). The target nucleic acid can be genomic, mitochondrial DNA, RNA or cDNA (col. 10, lines 19-20, col. 6, lines 33-34)(limitations of Claim 25-28). The genomic DNA samples are usually subject to amplification before application to an array (col. 10, lines 22-23)(limitations of Claims

16-17). Methods which amplify genomic DNA samples prior to application to the array have reduced the complexity of the genome.

Neither Sapolsky in view of Murphy nor Gentalen specifically teach detecting SNP using a multiwell dish. Neither Sapolsky in view of Murphy nor Gentalen specifically teach using a spacer sequence to attach the probe to the solid support.

However, Newton teaches oligonucleotides are immobilized to a microtitre dish (a multiwell dish) for analysis of SNPs (limitations of Claim 5). Newton teaches attaching probes to a solid phase via an amino link on the 5' end of the final T of the poly T region (col. 11, lines 60-65)(limitations of Claim 9-10).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to have modified the method of detecting numerous SNPs using an array with the teachings of Newton that an array of nucleic acids may be analyzed in separate wells of a multiwell dish. The ordinary artisan would have recognized that using a multiwell dish would ensure the detection of SNPs using a solid support much like an array.

Additionally, the ordinary artisan would have recognized that probes may be attached to solid support via an amino link on the 5' end of the final T of the poly T region. Addition of spacer sequences enable the detection of oligonucleotides. The spacer allows the target nucleic acid to be a distance from the solid support which allows for increased binding. Therefore, the ordinary artisan would have been motivated to have added the polyT tail to enable attachment to the solid support.

9. Claims 5, 8, 12-13, are rejected under 35 U.S.C. 103(a) as being unpatentable over Sapsolsky et al (US Pat. 5,858,659, January 1999) in view of Murphy et al. (WO 99/09164, February 25, 1999) as applied to Claims 1-4, 6-7, 11, 14, 16, 18, 19-22, 25, 27 above or Gentalen et al. (US Pat. 6,306,643, October 2001) in view of Walt et al. (U.S. Patent 6,327,410, December 4, 2001).

Gentalen teaches a method of using an array of probes in genetic analysis.

Gentalen teaches methods which use multiple cells in an array containing different pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55)(limitations of Claim 1, 2, 3, 4, 11, 14, 22, 23). The supports typically have discrete spatially addressable regions or cells (col. 11, liens 15-16). (limitations of Claim 6, 7). The target nucleic acid can be genomic, mitochondrial DNA, RNA or cDNA (col. 10, lines 19-20, col. 6, lines 33-34)(limitations of Claim 25-28). The genomic DNA samples are usually subject to amplification before application to an array (col. 10, lines 22-23)(limitations of Claims 16-17). Methods which amplify genomic DNA samples prior to application to the array have reduced the complexity of the genome.

Neither Sapsolsky in view of Murphy nor Gentalen does not specifically teach using surfaces such as multiwell dishes and beads.

However, Walt teaches a method of detecting target analytes using a surface which has been modified to contain physical configurations such as wells or small depressions in the substrate that can retain the beads such that a microsphere can rest in the well (col. 5, lines 60-65). As seen in Figure 5A and 5B, beads are located within a welled dish. Walt teaches that bioactive agents include nucleic acids. The nucleic acid may be DNA, both genomic and cDNA, RNA or any combination (col. 10, lines 30-33). Walt teaches that probes are designed to be complementary to a target sequence such that hybridization of the target and the probes of the present invention occurs (col. 10, lines 40-50). Each bead comprises a single type of bioactive agent (col. 11, lines 40-50). Walt teaches using different dyes which allow for distinguishing between molecules (col. 13). Walt teaches that the methodology finds uses in detection of mutations or mismatches in target nucleic acids such as single nucleotide polymorphisms (col. 24, lines 53-60). Walt teaches that the use of the beads with bioactive agents allows the beads to be randomly distributed on the array, a fast and inexpensive process as compared to either the in situ synthesis or spotting techniques of the prior art (col. 4, lines 53-56).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to have modified the array surface of Sapolsky in view of Murphy or Gentalen to contain wells and beads as taught by Walt. The ordinary artisan would have been motivated to have designed the array surface according to Walt since Walt teaches that "the use of the beads with bioactive agents allows the beads to be randomly distributed

on the array, a fast and inexpensive process as compared to either the in situ synthesis or spotting techniques of the prior art" (col. 4, lines 53-56).

10. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sapolsky et al (US Pat. 5,858,659, January 1999) in view of Murphy et al. (WO 99/09164, February 25, 1999) as applied to Claims 1-4, 6-7, 11, 14, 16, 18, 19-22, 25, 27 above or Gentalen et al. (US Pat. 6,306,643, October 2001) in view of Arnold et al. (U.S. Patent 6,410,231, June 25, 2002).

Gentalen teaches a method of using an array of probes in genetic analysis. Gentalen teaches methods which use multiple cells in an array containing different pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55)(limitations of Claim 1, 2, 3, 4, 11, 14, 22, 23). The supports typically have discrete spatially addressable regions or cells (col. 11, lines 15-16). (limitations of Claim 6, 7). The target nucleic acid can be genomic, mitochondrial DNA, RNA or cDNA (col. 10, lines 19-20, col. 6, lines 33-34)(limitations of Claim 25-28). The genomic DNA samples are usually subject to amplification before application to an array (col. 10, lines 22-23)(limitations of Claims

16-17). Methods which amplify genomic DNA samples prior to application to the array have reduced the complexity of the genome.

Neither Sapolisky in view of Murphy nor Gentalen specifically teach using four different labels for each of the ASO probes.

However, Arnold teaches methods of detecting single nucleotide polymorphisms (SNPs) by capturing probes which contain different labels. Arnold provides an example for simultaneously probing for n different SNPs on a target with m alleles each exploits  $n \times m$  differentially detectable labels. For example, for two SNPs each with two alleles, this embodiment exploit four differentially detectable labels measures as for instance, a Cy2/Cy7 ration for one SNP and a Cy3/Cy5 for the second SNP (col. 5, lines 35-45)(limitations of Claim 15).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to have modified the detection method of Sapolisky in view of Murphy or Gentalen with the teachings of Arnold to detect SNPs by using differential labels. The ordinary artisan would have been motivated to have used different labels for each distinct allele assayed for the expected benefit of ease of detection and definitive detection.

11. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over or Sapolisky et al (US Pat. 5,858,659, January 1999) in view of Murphy et al. (WO 99/09164, February 25, 1999) as applied to Claims 1-4, 6-7, 11, 14, 16, 18, 19-22, 25, 27 above or Gentalen et al. (US Pat. 6,306,643, October 2001) in view of Pinkel et al. (US Pat. 6,210,878, April 3, 2001).

Gentalen teaches a method of using an array of probes in genetic analysis. Gentalen teaches methods which use multiple cells in an array containing different pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55)(limitations of Claim 1, 2, 3, 4, 11, 14, 22, 23). The supports typically have discrete spatially addressable regions or cells (col. 11, lines 15-16). (limitations of Claim 6, 7). The target nucleic acid can be genomic, mitochondrial DNA, RNA or cDNA (col. 10, lines 19-20, col. 6, lines 33-34)(limitations of Claim 25-28). The genomic DNA samples are usually subject to amplification before application to an array (col. 10, lines 22-23)(limitations of Claims 16-17). Methods which amplify genomic DNA samples prior to application to the array have reduced the complexity of the genome.

Neither Sapolisky in view of Murphy nor Gentalen specifically teach using a reduced complexity genome.

However, Pinkel et al. (herein referred to as Pinkel) teaches an array based method which uses Cot-1 DNA to block repetitive sequences. Cot-1 is used to block the hybridization capacity of repetitive sequences.

Therefore, it would have been *prima facie* obvious to one of ordinary skill at the time the invention was made to have modified the haplotyping methods of Sapolisky in

view of Murphy or Gentalen to include an improved step of reducing the complexity of the genome, as taught by Pinkel. Pinkel teaches that hybridization capacity of repetitive sequences may be blocked using Cot-1 or human genomic DNA. The ordinary artisan would have been motivated to have blocked repetitive sequence to enable more sensitive detection. Prehybridization of the competitive Cot-1 DNA sequence will render the repetitive sequences unavailable for hybridization in the subsequent hybridization reaction to the array, thereby resulting in low background.

**12.** Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sapolsky et al (US Pat. 5,858,659, January 1999) in view of Murphy et al. (WO 99/09164, February 25, 1999) as applied to Claims 1-4, 6-7, 11, 14, 16, 18, 19-22, 25, 27 above or Gentalen et al. (US Pat. 6,306,643, October 2001)

Gentalen teaches a method of using an array of probes in genetic analysis. Gentalen teaches methods which use multiple cells in an array containing different pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55)(limitations of Claim 1, 2, 3, 4, 11, 14, 22, 23). The supports typically have discrete spatially addressable regions or cells (col. 11, lines 15-16). (limitations of Claim 6, 7). The target nucleic acid

can be genomic, mitochondrial DNA, RNA or cDNA (col. 10, lines 19-20, col. 6, lines 33-34)(limitations of Claim 25-28). The genomic DNA samples are usually subject to amplification before application to an array (col. 10, lines 22-23)(limitations of Claims 16-17). Methods which amplify genomic DNA samples prior to application to the array have reduced the complexity of the genome.

Neither Sapolisky in view of Murphy nor Gentelan specifically teaches using two different capture methods.

It is noted that, as written, the claims encompass performing the method twice using two different methods.

However, Caskey teaches a method of detecting single base extension reactions with a polymerase and terminating nucleotides, the terminating nucleotides being mutually distinguishable and observing the identity of the nucleotide to thereby analyze the sequence. The arrays may be "read" by determining the identity and the location of each terminating nucleotide within the array on the solid support. The label and position of each terminating nucleotide on the solid support directly defines the sequence of the polynucleotide of interest that is being analyzed.

Therefore, it would have been *prima facie* obvious to one of ordinary skill at the time the invention was made to have performed the method of Sapolisky in view of Murphy or the method of Gentelan in combination with the method of Caskey to confirm the results obtained in one of the methods. Performing two assays to determine the identity of a location provides a more confident result. The probe methods of Sapolisky and Gentelan require the hybridization of specific sequences, whereas the method of

Caskey requires the efficiency of a polymerase. Therefore, the two methods have different reagents and would allow for more confident results if the two methods were combined.

### ***Conclusion***

#### **13. No claims allowable over the art.**

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*J. Goldberg*  
Jeanine Goldberg  
June 6, 2003

*Gary Benzon*  
GARY BENZON, PH.D.  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600